A.6 EARLY INITIATION OF ENTERAL FEEDING

Recommendation and remarks

RECOMMENDATION A.6 (UPDATED)

Preterm and low-birth-weight (LBW) infants, including very preterm (< 32 weeks' gestation) and very LBW (< 1.5 kg) infants, should be fed as early as possible from the first day after birth. Infants who are able to breastfeed should be put to the breast as soon as possible after birth. Infants who are unable to breastfeed should be given expressed mother's own milk as soon as it becomes available. If mother's own milk is not available, donor human milk should be given wherever possible. *(Strong recommendation, moderate-certainty evidence)*

Remarks

- Enteral feeding includes direct breastfeeding and feeding by cups, naso- or orogastric tubes.
- The trials included in the systematic review mostly did not state the stability of the babies, so careful consideration is needed in applying these recommendations to unstable babies. The GDG considers that initiation of enteral feeding in unstable babies should be based on clinical judgement.
- Infants should be given mother's own milk wherever possible. The provision of colostrum is especially important. If mother's own milk is not available, then donor human milk should be given wherever possible. If human milk is not available, infants can be fed formula as this is preferable to delayed initiation of enteral feeding and the use of parenteral nutrition.
- There was no difference in effectiveness by volume of initial feed, so a recommendation was not made on restricting the volume of feed.
- In all but one of the trials, the control group received parenteral nutrition. The benefits of early initiation of enteral feeding may be even greater when the alternatives are intravenous fluids or dextrose water rather than parenteral nutrition.

Background and definitions

WHO and UNICEF recommend early initiation of breastfeeding within 1 hour of birth for all healthy term infants *(63)*. Clinicians continue to debate the optimal timing of feeding initiation for preterm and LBW infants for fear of potential health complications, including necrotizing enterocolitis *(13,82,83)*. Additionally, women in communities around the world may delay feeding due to the cultural practices of discarding colostrum, pain and discomfort after delivery, and concern about the developmental maturity of the infant, including the infant's inability to digest milk feeds *(84,85)*. In 2011, WHO recommended early initiation of enteral feeding for stable preterm or LBW infants *(19)*. However, there have been new studies since that time.

Summary of the evidence

OVERVIEW	A.6 Early initiation of enteral feeding
PICO	**Population** – Preterm or LBW infants **Intervention** – Early initiation of enteral feeding (< 72 hours) **Comparator** – Delayed initiation of enteral feeding (> 72 hours) **Outcomes** – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up
Timing, setting, subgroups	**Timing of the intervention** – Birth to 1 month of age **Setting** – Health-care facility or home in any country or setting **Subgroups** • Gestational age at birth (< 32 weeks, ≥ 32 weeks) • Birth weight (< 1.5 kg, ≥ 1.5 kg) • Timing of feed initiation (days 1, 2, 3) • Milk volume (< 15 ml/kg per day, ≥ 15 ml/kg per day) • Milk type (human milk, formula, and mixed human milk with formula)

Effectiveness: Comparison – Early versus delayed initiation of enteral feeding

Sources and characteristics of the evidence

The effectiveness evidence was derived from a systematic review of 14 trials enrolling 1511 preterm or LBW infants, which compared early initiation of enteral feeding (< 72 hours) with delayed initiation of enteral feeding (≥ 72 hours). The trials were from nine countries (Canada, Chile, Colombia, India, the Netherlands, Spain, the United Arab Emirates, the United Kingdom and the USA) *(86)*. All trials were based in hospital NICUs. Ten trials restricted enrolment to very preterm infants (< 32 weeks' gestation) or VLBW infants (< 1.5 kg) and five enrolled all preterm or LBW infants. Three studies enrolled only small-for-gestational-age (SGA) infants. Early initiation time ranged from 1 to 3 days after birth and delayed initiation time ranged from 4 to 15 days after birth. Two studies initiated feeding by day 1 (i.e. < 24 hours), eight studies initiated by day 2 (i.e. < 48 hours) and five studies initiated by day 3 (i.e. < 72 hours). Enteral feed volumes ranged from 5 to 25 ml/kg per day. Only two studies provided babies with feed volumes > 15 ml/kg per day. Only one trial provided direct breastfeeding while the remaining 13 gave feeds by naso- or orogastric tube. Three studies gave the babies formula milk, one gave mother's own milk and the remaining 10 gave a mixture of milks (i.e. mother's own, donor human milk and/or formula). All infants received supplemental parenteral nutrition in the delayed initiation group, except for one study which did not specify.

Critical outcomes

For early feeding compared with delayed feeding for preterm or LBW infants, 12 studies reported all-cause mortality outcomes, 14 reported morbidity (14 reported necrotizing enterocolitis, 6 sepsis, 1 intraventricular haemorrhage), 7 reported growth outcomes (7 reported time to regain birth weight, 1 weight, 1 length and 3 head circumference). None of the trials reported on neurodevelopment. (Full details are provided in GRADE Table A.6, in the Web Supplement.)

- **Mortality**: Moderate-certainty evidence from 12 trials totalling 1292 participants suggests a decrease in all-cause mortality by hospital discharge (RR 0.69, 95% CI 0.48 to 0.99).
- **Morbidity:** Low-certainty evidence from 13 trials totalling 1484 participants suggests little or no effect on necrotizing enterocolitis by hospital discharge (RR 1.05, 95% CI 0.75 to 1.46). Low-certainty evidence from five trials totalling 626 participants suggests little or no effect on sepsis by discharge (RR 0.90, 95% CI 0.54 to 1.52). Very-low-certainty evidence from one trial with 84 participants suggests a decrease in intraventricular haemorrhage by hospital discharge (RR 0.48, 95% CI 0.18 to 1.25).
- **Growth:** Low-certainty evidence from seven trials totalling 569 participants suggests little or no effect on time to regain birth weight (in days) (MD 0.26, 95% CI -0.63 to 1.15). Low-certainty evidence from three trials totalling 142 participants suggests little or no effect on weight (in grams) at latest follow-up (at chronological age 6–12 weeks) (MD -49.02, 95% CI -149.62 to 51.61). Very-low-certainty evidence from one trial with 40 participants suggests an increase in weight gain (in grams) from enrolment to 30 days follow-up (MD 51, 95% CI 32.4 to 69.6). Low-certainty evidence from two trials totalling 82 participants suggests little or no effect on length gain (in centimetres) at latest follow-up (at chronological age 32 weeks) (MD -0.62, 95% CI -1.51 to 0.27). Very-low-certainty evidence from two trials totalling 82 participants suggests little or no effect on head circumference (in centimetres) at latest follow-up (at discharge or chronological age 32 weeks) (MD -0.56, 95% CI -1.18 to 0.06).

Other outcomes

There was little or no effect on feed intolerance at discharge (RR 1.03, 95% CI 0.66 to 1.60; 2 trials, 187 participants) or length of hospital stay (days to discharge) (MD -3.2, 95% CI -5.74 to -0.66; 10 trials, 1100 participants).

Subgroup analyses

For the analyses by gestational age and birth weight, subgroup differences could not be assessed as there were insufficient studies on any critical outcome.

Values and acceptability

The systematic review about what matters to families about the care of the preterm or LBW infant (see Table 1.1) reported that families want to be involved in delivering care to infants, including supporting nutrition, and want to take an active role in deciding what interventions are given to infants, including what and how they are fed *(14)*. There have been studies of the barriers, facilitators, preferences, values and acceptability of early and late initiation of enteral feeding for preterm or LBW infants *(84,85)*. Reasons for delay in initiation of feeding include cultural practices of discarding colostrum, pain and

discomfort after delivery, and concern about the developmental maturity of the baby, including the baby's inability to digest milk feeds. Reasons for early initiation include the importance of providing nurturing care to the baby as soon as possible, and concerns about the use of intravenous lines, dextrose water, total parenteral nutrition and lack of other nutritional support *(84,85)*.

Resources required and implementation considerations

Organization of care

Early initiation of enteral feeding from the first day of life (the day of birth) can be implemented at home and at all levels of newborn care (primary, secondary and tertiary).

Infrastructure, equipment and supplies

National or local guidance for health-care facilities should be used.

Workforce, training, supervision and monitoring

Health workers at all levels can provide early initiation support to mothers and families. Standardized packages are needed for training, supervision and monitoring.

Feasibility and equity

There was no specific evidence on the feasibility and equity of early initiation of feeding for preterm or LBW infants.

Summary of judgements

Comparison: Early vs delayed initiation of enteral feeding (A.6)	
Justification	• Evidence of moderate benefits: decreased mortality *(moderate-certainty evidence)*, decreased length of hospital stay *(moderate-certainty evidence)*, decreased intraventricular haemorrhage *(very-low-certainty evidence)* • No evidence of harms • Evidence of little or no effect on: necrotizing enterocolitis *(low-certainty evidence)*, sepsis *(low-certainty evidence)*, growth, i.e. time to regain birth weight, weight in grams, weight gain in grams, length at discharge *(low- to very-low-certainty evidence)*, feed intolerance *(low-certainty evidence)* • No evidence on other critical outcomes

Evidence-to-Decision summary	
Benefits	Moderate
Harms	Trivial or none
Certainty	Moderate
Balance	Favours early initiation
Values	No uncertainty or variability about outcomes
Acceptability	Acceptable
Resources	Negligible
Feasibility	Feasible
Equity	Equitable